25. A method according to Claim 24, wherein the monoclonal antibody is that secreted by the hybridoma cell line deposited at the CNCM under Accession No. I-1397.

26. A pharmaceutical composition comprising, as an active ingredient, an effective amount of a monoclonal antibody according to Claim 19, and a physiologically acceptable carrier.

27. A pharmaceutical composition according to Claim 26, wherein the antibody is that secreted by the hybridoma cell line deposited at the CNCM under Accession No. I-1397.--

REMARKS

Amendment of the Claims

Claims 1-18 have been replaced with new claims 19-27.

New claim 19 replaces original claims 1-3. Claim 19 is restricted to either the I-1397 antibody or a monoclonal antibody having the same antigen binding characteristics. Such a restriction overcomes the Examiner's objections raised in paragraphs 8a and 8b, as well as in paragraphs 10a-c of the Office Action.

New claims 20-23 correspond to original claims 4, 5, 6 and 8, respectively.

New method claim 24, restricted to the treatment of cancer, replaces original broad method claim 9.

Original claims 7, 10 and 11 were canceled to overcome the Examiner's objection raised in paragraphs 10d-e of the Office Action.

Original pharmaceutical composition claim 14 was also canceled to overcome the Examiner objection raised in paragraph 10d of the Office Action.

Original claim 16 was canceled to overcome the Examiner's objections in paragraphs 10f-h and 11 of the Office Action.

Original claims 17 and 18 were previously withdrawn in response to a restriction requirement.

The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

Objection of Specification under 35 U.S.C. § 112, ¶ 1

The specification has been objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

As the basis of this objection, the Examiner states:

> The specification lacks complete deposit information for the deposit of the hybridoma cell line CNCM Accession No. I-1397. It is not clear that hybridoma cell lines and monoclonal antibodies possessing the identical

properties of I-1397 and the monoclonal antibodies that it secretes are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive antibodies and hybridomas identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed hybridoma cell line and monoclonal antibody, a suitable deposit of the cell line for patent purposes, evidence of public availability of the claimed cell line or evidence of the reproducibility without undue experimentation of the claimed hybridoma, is required.

Applicant's referral to the deposit of I-1397 on page 7 of the specification is an insufficient assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposits are made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by the International Depository Authority under the provisions of the Budapest Treat, that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State

* * *

> Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

As required by the Examiner in paragraph 6 of the Office Action, applicants submit herewith a Declaration by Dr. Fischman, the Managing Director of Mor-Research Applications Ltd. regarding the deposit of the hybridoma cell line I-1397 at the CNCM.

Applicants also submit herewith a copy of the official receipt from the CNCM depository.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is unnecessary as that information already appears in the specification on page 7, paragraph 3.

The Declaration by Dr. Fischman and the official receipt provide adequate assurance that all required deposits have been made and all the conditions of 37 CFR 1.801-1.809 have been met, thereby satisfying the requirements under 35 U.S.C. § 112, first paragraph.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this objection.

Objection of Specification under 35 U.S.C. § 112, ¶ 1

The specification has been objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure.

As the basis of this rejection, the Examiner states:

> The specification does not adequately teach how to make and use the claimed antibodies as broadly claimed. Those of skill in the art would not known how to effectively make and use the claimed methods with a reasonable expectation of success based on the teachings of the specification and the evidence of record.
>
> a. Claims 1-3, 5-7,9-11, 13-14 and 16 are drawn to monoclonal antibodies that bind to any unspecified antigen on B lymphoblastoid cells. The specification exemplifies only one such monoclonal antibody, the BAT-1 monoclonal antibody, in support of the broad claims. This antibody recognizes a 48-50 kD protein, increases thymidine incorporation in human peripheral blood lymphocytes (p.19), induces cytotoxic lysis of tumor cells (p.22) and exhibits an anti-tumor effect in the model systems of lung metastases of MCA fibrosarcoma, B16 melanoma and 3LL tumor cells in the C57BL and BALB/c mice (see p.27). The nature of the antigen recognized by antibodies of the invention is presumably critical in terms of the immunostimulatory property of the exemplary antibody. One can not extrapolate from the single antigen-antibody system disclosed to the production of immunostimulatory antibodies that bind to other B lymphoblastoid cell antigens. The specification provides no direction or guidance with respect to the identification of antibodies having different antigen-binding specificities which have immunostimulatory properties without undue experimentation.
>
> b. Claim 1 is broadly drawn to "immunostimulatory" antibodies. The specification exemplifies antibodies that mediate only the specific immunostimulatory effects previously discussed in paragraph 8a above. Absent a more specific and detailed description in applicant's specification of how to effectively identify the

immunostimulatory antibodies, undue experimentation would be required to make and use the claimed invention with a reasonable expectation of success.

c. Claim 10 is broadly drawn to a method for the treating of a "disease or disorder". The specification does not teach how to treat diseases or disorders commensurate with the scope of the claim. While the specification contemplates that the diseases or disorders to be treated according to the claimed methods include HIV infection, various autoimmune diseases and some genetic and acquired immunodeficiencies (p. 8, lines 21-26), it does not teach how to effectively treat HIV-1 infections, various autoimmune diseases and genetic and acquired immunodeficiencies. The only in vitro working example exemplified in the specification is directed to the treatment of tumors in experimental mice. This example can not be extrapolated to HIV-1 infection and autoimmune diseases, which differ widely in their etiologies and pathobiology. The class of diseases which are broadly categorized as autoimmune diseases includes numerous diseases of diverse underlying etiologies and disease mechanisms, whose pathologies are complex and, in most cases, incompletely understood. Thus, the specification does not set forth sufficient teachings to allow one skilled in the art to practice the claimed invention with a reasonable expectation of success. One of skill in the art could not predict the efficacy of the claimed methods for treatment of diseases or disorders other than the murine lung metastasis model on the basis of the evidence of record.

d. Claims 1, 2 and 10 are drawn to the treatment of tumors and cancer, and can be broadly interpreted to read on the treatment of human tumors. The present invention pertains to the experimental and unpredictable area of the in vivo treatment of human tumors by the administration of immunoglobulins. The difficulties associated with the development of effective antibody-based therapies for human cancers are well established in the art. The example provided in the specification, the antitumor effect of the claimed monoclonal antibodies in the model systems of lung metastases of MCA fibrosarcoma, B16 melanoma and 3LL tumor cells in the C57BL and BALB/c mice (see p. 27) does not provide sufficient basis to predict the efficacy of the disclosed method for the treatment of human tumors.

> The specification provides insufficient evidence that the claimed methods are effective for treatment of human tumors. The claimed invention has been exemplified in methods of administering the claimed monoclonal antibody to tumor-bearing mice. However, as evidenced by Osband and Ross (Immunology Today 11:193-195, 1990), the mouse is not an art-recognized animal model which is predictive of the efficacy of immunotherapeutic agents in humans. Osband and Ross teach that the response of animals of immunotherapy is not predictive of their effects in human patients. Due to the extreme complexity of the host-tumor immunorelationship, animals to not fully mimic the biology of human patients with cancer and the immune systems of animals and humans differ such that immunotherapeutic agents fail to demonstrate comparable activity in animals and humans. (See the paragraph bridging page 192-193). Those of skill in the art would not predict the ability to effectively use the claimed methods for treating human tumors on the basis of the evidence of record.
>
> e. Claim 16 is drawn to an agent other than the claimed monoclonal antibody which is capable of enhancing the activity of the cytotoxic lymphocytes, or broadly interpreted, enhancing the immunostimulatory effect obtained in claim 1, in a synergistic manner. The specification teaches only the one such agent, I1-2 (p.22). No description of the physical, chemical or pharmacological characteristics of such other agents is provided. Absent a specific and detailed description in the specification of how to effectively make and use the agents as broadly claimed undue experimentation would be required to practice the claimed methods with a reasonable expectation of success.

The foregoing amendments replacing original claims 1-18 with new claims 19-27 obviate the rejections raised in paragraphs 8a-c of the Office Action.

Applicants respectfully traverse the rejections raised in paragraphs 8d-e of the Office Action regarding the effectiveness of the claimed invention in treating human tumors.

In paragraph 8d of the Office Action, the Examiner rejected the claims on the ground that the specification provides experimental data only with respect to the mouse tumor model and cited a single publication (Osband and Ross) in support of the fact that the response of animals to immunotherapy is not predictive to the effect of the immunotherapy in human patients.

The Commissioner's new examination guidelines for biotech applications states *inter alia*:

> Examiners are reminded that they must treat as true credible statements made by an applicant or a declarant in a specification or in a declaration provided under 37 CFR § 1.132, unless they can show that one of ordinary skill in the art would have a rational basis to doubt the truth of such statements. 60 Fed. Reg. 97 (1995); 49 Patent, Trademark & Copyright Journal (BNA) No. 1210 (Jan. 5, 1995) (emphasis added).

The Examiner's single citation of the publication by Osband and Ross does not constitute a showing that one of ordinary skill in the art would have reasonable basis to doubt the truth of statements made by applicants in the specification regarding the therapeutic utility of the monoclonal antibody in humans. It is clear that the Examiner is requiring to limit the claims to the exemplified embodiment without providing sufficient evidence or reasoning to rebut the presumptively accurate statements in the specification that the present invention is operable also for the treatment of cancer in humans.

In addition, the Examiner states that those of ordinary skill

in the art could not predict the ability to effectively use the claimed methods for treating human tumors on the basis of the evidence of record. Applicants respectfully submit that such an extrapolation from a mouse experimental model to treatment of humans is the basis of a very large proportion of all inventions and patent applications in the field of human medicine. By their nature, inventions in the field of human medicine take many years to develop. It is accepted law and practice that results obtained from an animal model form a fair basis for claims directed to means for the treatment of humans. This is not to say that animals fully mimic the biology of the human patients with cancer, or that the immune systems of animals and humans are completely comparable in activity. However, against the one citation provided by the Examiner, tens if not hundreds of scientific publications as well as accepted patent applications in this field may be cited in which preliminary experiments in animals were indeed predictive, at least generally, of the results obtained later in humans. It should be appreciated by the Examiner that it is very difficult to carry out experiments in humans at a preliminary stage in which a patent application is usually filed, mainly since in order to conduct such experiments it is necessary to go through a very laborious process of approval. An approval to conduct such experiments is largely based on preliminary experiments in animals.

The courts have repeatedly held that proof of an alleged pharmaceutical property for a compound by statistically significant tests with standard experimental animals is sufficient to establish utility.

> [I]t is our firm conviction that one who has taught the public that a compound exhibits some desirable pharmaceutical property in a standard experimental animal has made a significant and useful contribution to the art, even though it may eventually appear that the compound is without value in the treatment of humans...Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. In re Brana, 34 USPQ 2d 1436, 1442, citing In re Krimmel, 292 F.2d 948, 953, 130 USPQ 215, 219.

In addition, the PTO Legal Analysis Supporting Utility Examination Guidelines acknowledges the same standard.

> If reasonably correlated to the particular therapeutic or pharmacologic utility, data generated using *in vitro* assays, or from testing in an animal model or a combination thereof almost invariably will be sufficient to establish therapeutic or pharmacological utility for a compound, composition, or process...Data from any test that the applicant reasonably correlates to the asserted utility should be evaluated substantively. Thus, an applicant may provide data generated using a particular animal model with an appropriate explanation as to why that data supports the asserted utility...Thus, if one skilled in the art would accept the animal tests as being *reasonably predictive* of utility in humans, evidence from those tests should be considered sufficient to support utility. *Legal Analysis*, § III.C.

The standard of review of utility under 35 U.S.C. § 101 for therapeutic inventions is equivalent to that under 35 U.S.C. § 112.

See footnote 61 of the Legal Analysis.

Finally, applicants have obtained new experimental results showing the anti-tumor activity of the MAb of the invention in mice bearing human tumors. Additionally, results showing that the MAb of the invention is capable of inducing human tumor regression mediated by stimulation of human immunocytes (obtained in SCID mice) are also available. These results strongly support the ability of the claimed methods to effectively treat human tumors on the basis of the evidence of record contrary to the Examiner's statement in paragraph 8e of the Office Action. Applicants intend to present these results in a Declaration to be prepared and submitted in the near future.

Rejection of Claims 1-16 under 35 U.S.C. § 112, ¶ 1

Claims 1-16 have been rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Applicants respectfully traverse this rejection for reasons set forth in response the objection to the specification, herein incorporated by reference to avoid repetition.

Accordingly applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 1-16 under 35 U.S.C. § 112, ¶ 2

Claims 1-16 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

As the basis of this rejection, the Examiner states:

> a. Claim 1 is vague and indefinite in the recitation of "immuno-stimulatory". It is unclear whether activation and/or proliferation of lymphocytes or other immuno-stimulatory effects are claimed. Thus the metes and bounds of the claim are unclear.
>
> b. Claim 1 and 2 are vague and indefinite in the recitation of "elicits anti-tumor effect". Tumors have many biological and pathological effects. For example; growth in mass, metastases, cachexia and angiogenesis. The particular anti-tumor effect claimed is unknown. Thus, the metes and bounds of the claim are unclear.
>
> c. Claim 2 recites an improper Markush group. The applicant is referred to MPEP § 706.03(y) and advised to reformat the claim to read "wherein R is a material selected from the group consisting of A, B, C, and D", or "wherein R is A,B,C, or D".
>
> d. Claims 3, 7, 11 and 14 are vague and indefinite in the recitation "having the characteristics of". The specific characteristics referred to are unknown.
>
> e. Claim 9 is vague and indefinite in the recitation "disease or disorder". The particular diseases or disorders to be treated with the claimed antibodies are not known. How a disease differs from an disorder is unknown.
>
> f. Claim 16 is vague and indefinite in the recitation "an agent other than said antibody". The identity of the agents other than said antibody is unknown and thus, the metes and bounds of the claim are unknown.
>
> g. Claim 16 is vague and indefinite in the recitation "the cytotoxic lymphocytes", which lacks antecedent basis.
>
> h. Claim 16 is vague and indefinite in the recitation "enhancing the activity of", as it is unclear what specific

activities are enhanced.

The foregoing amendments replacing original claims 1-18 with new claims 19-27 obviate this rejection.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Objection of Claim 16 for Informalities

Claim 16 has been objected to because of informalities in the recitation of "an an".

The foregoing amendment canceling claim 16 obviates this rejection.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 1-2, 5-6, 9-10, 13 and 16

under 35 U.S.C. § 102(b)

Claims 1-2, 5-6, 9-10, 13 and 16 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Brown et al. (Blood 73:651-661, 1989).

As the basis of this rejection, the Examiner states:

> Brown discloses a monoclonal antibody for anti-tumor uses that is the same as that claimed in claims 1-2, 5-6, 9-10, 13 and 16. This monoclonal antibody is obtained by immunizing an animal with B lymphoblastoid cells, binds to B Lymphoblastoid cells and induces proliferation and activation of peripheral blood lymphocytes (p. 655,

> column 2, two patients made an immune response against mouse immunoglobulin after administration of the monoclonal antibody, which is immuno-stimulation). Brown also discloses the hybridoma cell line that produces said monoclonal antibody, the strong anti-tumor effect of said monoclonal antibody and the use of the monoclonal antibody with other agents capable of enhancing its activity, in this case I1-2.

Applicants respectfully traverse this rejection.

Brown et al. disclose the preparation of monoclonal antibodies raised against lymphoma cells obtained from various lymphoma patients. The antibodies are directed against the idiotype of the immunoglobulin present on the surface of the B-cells which varies from patient to patient. For each patient, Brown et al. prepared a different anti-idiotype antibody which was capable of binding to the immunoglobulin present on the cell surface of the lymphoma cell in that patient.

In contrast to Brown et al., the present invention relates to an anti-B lymphoblastoid antibody which does not bind the cell surface immunoglobulin, but rather was surprisingly shown to bind normal T-cells of the immune system. The antibody is capable of activating a lymphocyte which, when transferred into animals carrying various tumors, show an anti-tumorigenic effect. The Examiner indicated in brackets, in paragraph 13 of the Office Action that "two patients made an immune response against mouse immunoglobulin after administration of the monoclonal antibody,

which is immuno stimulation". However, the response of the two patients was in fact the production of human anti-mouse antibody (HAMA) which is a known negative response of humans against mouse antibodies and, contrary to the Examiner's comment, does not constitute evidence for immuno stimulation.

Based on the foregoing, Brown et al. do not anticipate claims 1-2, 5-6, 9-10, 13 and 16.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 1-2, 5-6, 9-10, 13 and 16

under 35 U.S.C. § 102(b)

Claims 1-2, 5-6, 9-10, 13 and 16 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Ledbetter (U.S. Patent No. 5,182,368), January 26, 1993).

As the basis of this rejection, the Examiner states:

> Ledbetter discloses an immunostimulatory monoclonal antibody for anti-tumor uses that is the same as that claimed in claims 1-2, 5-6, 9-10, 13 and 16. This monoclonal antibody is obtained by immunizing an animal with B lymphoblastoid cells (col. 8, lines 63-67), binds to B Lymphoblastoid cells and induces proliferation and activation of peripheral blood lymphocytes (abstract). Ledbetter also discloses the hybridoma cell line that produces said monoclonal antibody, the use of said monoclonal antibody for the treatment of diseases and disorders (col. 4, lines 17-26) including anti-tumor treatments (col.4, lines 27-42), a pharmaceutical composition containing the monoclonal antibody (see col.16, lines 51-54) and the use of the monoclonal

antibody with other agents capable of enhancing its activity (see col. 13, lines 20-27).

Applicants respectfully traverse this rejection.

The antibody disclosed by Ledbetter (hereinafter "the Ledbetter antibody") differs from the antibody of the present invention in the following:

(a) The Ledbetter antibody induces proliferation of B-cells, while the antibody of the present invention induces proliferation of T-cells.

(b) The Ledbetter antibody itself (anti-Bp50) is not capable of activating or inducing proliferation of B-cells by itself, but rather requires additional other antibodies as is the case in growth factor induced proliferation and activation. By contrast, the antibody of the present invention directly induces proliferation of cells with no need for additional antibodies.

(c) The Ledbetter antibody is directed against a 50 kDa determinant which is specific for B-cells, while the antibody of the present invention binds T-cells as well as other cells including NK cells.

While Ledbetter et al. prepared antibodies against receptors present on normal B-cells, in accordance with the present invention, B-blastoid cells were used for immunization, resulting surprisingly in an antibody which is capable of binding to non-activated non-B-cells. In addition, Ledbetter used the monoclonal

antibody for the direct treatment of B-cells or malignancies of B-cells which comprise the Bp50. By contrast, the antibody of the present invention is used for the treatment of solid tumors which are completely different tumors than the ones described by Ledbetter.

Based on the foregoing, Ledbetter does not anticipate claims 1-2, 5-6, 9-10, 13 and 16.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 3-4, 7-8, 11-12 and 14-15
under 35 U.S.C. § 102(b) or, in the alternative,
under 35 U.S.C. § 103

Claims 3-4, 7-8, 11-12 and 14-15 have been rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Ledbetter (U.S. Patent No. 5,182,368, filed May 24, 1991).

As the basis of this rejection, the Examiner states:

> For this analysis, the recitation in claim 3, "having the characteristics of the monoclonal antibody produced by the hybridoma cell line ... CNCM No. I-1397," is broadly interpreted to be a monoclonal antibody with the same physical properties as those disclosed in the specification for CNCM No. I-1397, also called the BAT-1 Mab. Thus, a monoclonal that identifies a binds a 48-50kD protein (p. 7) on cells of B lineage. Ledbetter discloses an immunostimulatory monoclonal antibody, that recognizes a polypeptide of approximately 50 Kd (see p.

> 18, lines 45-46), with the properties previously discussed in paragraph 15, above that is the same as that claimed in claims 3.

The foregoing amendments replacing claim 3 with new claim 19 obviates this rejection.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

Rejection of Claims 3-4, 7-8, 11-12, 14-15 under 35 U.S.C. § 103

Claims 3-4, 7-8, 11-12, 14-15 have been rejected under 35 U.S.C. § 103 as being unpatentable over Hoskin et al. (Cancer Immunol. Immunother. 29:226-230, 1989) in view of Ledbetter.

As the basis of this rejection, the Examiner states:

> Hoskin et al. teaches the use of an immunostimulatory monoclonal antibody to induce proliferation and activation of peripheral blood lymphocytes. This antibody, when injected into tumor-bearing mice, elicits an anti-tumor effect (see abstract). Hoskin does not teach an antibody that recognizes a 50 Kd protein on B lymphoblastoid cells. However, the teachings of Ledbetter, disclosing an immunostimulatory monoclonal antibody that recognizes a polypeptide of approximately 50 Kd (see p. 18, lines 45-46), have been previously discussed in paragraph 15 above.
>
> It would have been prima facia obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the monoclonal antibody taught by Ledbetter in the anti-tumor method taught in Hoskin et al. one of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Hoskin, that the in vivo activation of cytolytic cells with anti-tumor activity by antibodies holds potential as an alternative form of cancer treatment (p. 299).

Applicants respectfully traverse this rejection.

The antibody described by Hoskin et al. (hereinafter "the Hoskin antibody") is directed against a T-cell receptor which is the primary target for activation of these cells. By contrast, the B-lymphoblastoid Daudi cells used in the present invention lack a T-cell receptor and are, thus, different than the Hoskin antibodies. In addition, the Hoskin antibody induces activation of effector cells which are non-MHC restricted, whereas the antibody of the present invention acts as a second signal following activation by the tumor itself.

For the reasons discussed above, Ledbetter does not overcome the deficiencies of Hoskin et al.

Based on the foregoing, neither Hoskin et al. nor Ledbetter, whether alone or combined, teaches or suggests the claimed invention. Furthermore, there is no suggestion or motivation for combining or modifying the references' teachings to arrive at the claimed invention. The only way that the Examiner could have arrived at the claimed invention was by picking and choosing among isolated disclosures in the prior art based on applicants' teachings in the present application. This is hindsight reconstruction which is impermissible in a § 103 determination. In re Fritch, 23 USPQ.2d 1780, 1784 (Fed. Cir. 1992); In re PIasecki, 745 F.2d 1468, 233 USPQ 785 (Fed. Cir. 1984).

It is clear from the above discussion that the claimed invention is indeed a significant one. The invention fills a critical need that has heretofore existed in biotechnology, solving problems that went unsolved in others' hands despite the availability of the literature to which the Examiner's rejections refer. Applicants therefore submit that the claimed invention is patentable over Hoskin et al. in view of Ledbetter.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this rejection.

CONCLUSION

Based upon the above amendments and remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw the rejections of claims 1-16 and allow all pending claims presented herein for reconsideration. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

PATENT
Attorney Docket No. 22671

The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES

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